

First Documentation of *Rickettsia conorii* Infection (Strain Indian Tick Typhus) in a Traveler

To the Editor: Spotted fever group rickettsiae are gram-negative intracellular bacilli associated with arthropods, mainly ticks, as vectors. To date, 12 tick-borne rickettsioses are recognized worldwide, seven since 1991 (1). Indian tick typhus (ITT) is a tick-borne rickettsiosis prevalent in India (1).

Although the disease has been recognized clinically, cases have been documented only rarely, and then mainly with nonspecific serologic tools, such as the Weil Felix test. We report the first serologically documented case of infection caused by *Rickettsia conorii* (strain ITT) in a French traveler returning from India.

In September 1999, a 25-year-old woman living in France was hospitalized with a 4-day history of fever, headache, vertigo, malaise, and disturbance of vision, followed 3 days later by arthromyalgia and a rash. On the day of admission, she had returned from a 1-month stay in India. She reported a number of bites by unidentified arthropods during her trip. Her temperature was 40°C with relative bradycardia (72/minute). Physical signs included pharyngitis, transient epistaxis, bilateral conjunctivitis, and a maculopapular rash including petechiae, mostly on the trunk and lower limbs but also on her palms and the soles of her feet. There was no inoculation eschar.

Clinical laboratory findings included increased alanine aminotransferase (56 UI/L), lactate dehydrogenase (1,008 UI/L), C-reactive protein (130 mg/L), and erythrocyte sedimentation rate (74 mm/hour). The kaolin cephalin time was 43 seconds (control 34 seconds). Hemoglobin was 10.5 g/dL, and the mean corpuscular volume was 99.7 fl. Repeated blood smears, blood cultures, and a stool bacterial culture disclosed no pathogens. Serologic tests, including assays for rickettsioses, were negative.

The patient received 5 days of empirical doxycycline treatment (200 mg/day), intravenously for the first 2 days because of vomiting. She became afebrile 2 days after therapy was begun. Subsequently, all her symptoms resolved. Ten days later, the immunofluorescence assay for antibodies reactive with spotted fever group rickettsiae showed increased levels of immunoglobulin (Ig) M (1:256) and IgG (1:1024) against *R. conorii* Seven and IgM (1:512) and IgG (1:2048) against *R. conorii* ITT. Serologic findings were completed by Western blot performed with acute-phase serum, which showed a band of approximately 135 kDa against *R. conorii* ITT, but not *R. conorii* Seven. Cross-absorption studies were performed with convalescent-phase sera. Sera were absorbed with *R. conorii* Seven and *R. conorii* ITT antigens and then tested by immunofluorescence assay for remaining antibodies reactive to both antigens. When absorption was performed with *R. conorii* ITT antigens, serologic testing was negative for antibodies to both *R. conorii* Seven and *R. conorii* ITT antigens. However, when absorption was done with *R. conorii* Seven antigens, subsequent serologic testing was negative for antibodies to *R. conorii* Seven, but antibodies to *R. conorii* ITT remained (1:100). Thus, Western blotting and cross-absorption strongly supported that the infection was due to *R. conorii* ITT.

Although ITT was clinically described at the beginning of the century, the etiologic agent has never been isolated from patients in India, nor has a case been diagnosed by

strain-specific serologic testing. A spotted fever group rickettsia was isolated in 1950 from a brown dog tick, *Rhipicephalus sanguineus*, collected in India (2) and assumed to be the agent causing ITT. It was designated as *Rickettsia conorii*, the agent of Mediterranean spotted fever, which occurs all around the Mediterranean and is transmitted by the same tick species. However, the disease as it appears in India differs from the common description of Mediterranean spotted fever. The rash is frequently purpuric, and an inoculation eschar at the bite site is rarely found, as in this case. The disease as known in India is mild to moderately severe, although our case may be considered severe (1,3,4).

Strain differences within the species *R. conorii* may account for differences in clinical presentation. Although different isolates of *R. conorii* can be distinguished antigenically (5-7), molecular taxonomic methods demonstrated recently that these rickettsiae are closely related and cluster together (8-10). Thus, the species is considered by many as *R. conorii*, including four serovars: *R. conorii* with three type strains, Seven being the one most commonly identified in our laboratory in isolates from France, Portugal, North Africa (D. Raoult, unpub. data), Kenya, and Morocco (apparently a unique isolate); *R. conorii* Indian tick typhus; *R. conorii* Astrakhan, and *R. conorii* Israel.

Immunofluorescence is the reference diagnostic method for associated rickettsioses, but cross-reactivity among related isolates confounds interpretation of serologic tests. Cross-absorption tests, especially in conjunction with Western blot immunoassays, can be used to determine the rickettsia species involved, as reported in this case. The higher sensitivity of Western blots compared with immunofluorescence has been demonstrated previously in our laboratory; it is frequently positive in acute-phase sera when antibodies cannot be detected by immunofluorescence (11). In this case, we used *R. conorii* Seven as the type strain of *R. conorii* because it is most closely related to *R. conorii* ITT phylogenetically (10). Although these techniques are time-consuming and available only in specialized reference laboratories, they provide data of importance that allow a better understanding of the epidemiology of rickettsioses.

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